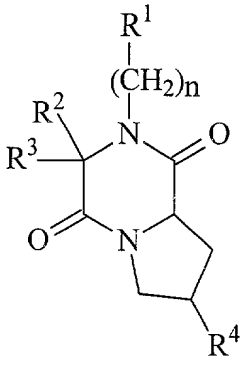
CLAIMS

What is claimed is:

1. A compound of the structure (I):



(I)

and optical isomers, diastereomers, enantiomers and pharmaceutically acceptable salts thereof in isolation or mixture, where, independently at each location:

R^1 is an aryl or heteroaryl ring;

R^2 and R^3 are selected from hydrogen, alkyl, heteroalkyl, aryl, heteroaryl, carbocycle aliphatic ring, and heterocycle aliphatic ring;

n is 1, 2 or 3;

R^4 is selected from $-OR^5$ and $-NR^6R^7$,

R^5 is selected from hydrogen, alkyl, heteroalkyl, aryl, heteroaryl, carbocycle aliphatic ring and heterocycle aliphatic ring; and

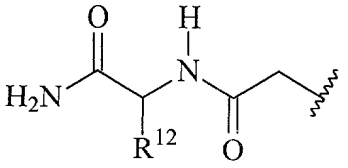
R^6 and R^7 are independently selected from hydrogen, alkyl, heteroalkyl, aryl, heteroaryl, carbocycle aliphatic ring and heterocycle aliphatic ring or R^6 and R^7 taken together with the nitrogen atom to which they are attached form a heterocycle aliphatic ring.

2. A compound of claim 1 wherein R^1 is phenyl and the phenyl is substituted with 1-4 substituents independently selected at each occurrence from alkyl, heteroalkyl, aryl, heteroaryl, carbocycle aliphatic ring, heterocycle aliphatic ring.

3. A compound of claim 2 wherein R^1 is phenyl having a substituent at the position *para* to the site of attachment to the piperazine ring.

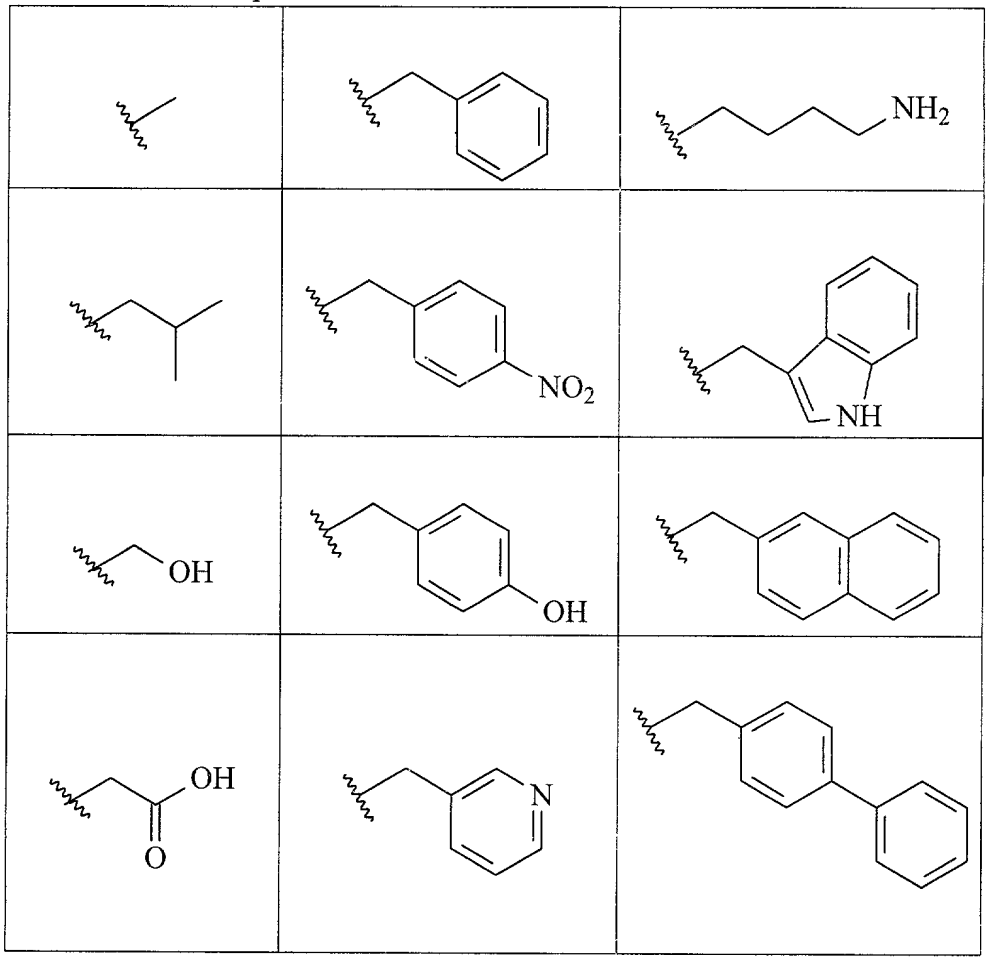
4. A compound of claim 3 wherein R^1 is phenyl having a substituent at the position *para* to the site of attachment to the piperazine ring, and the substituent has the formula R^{10}-R^9-R^8-, wherein R^8 is selected from direct bond, alkylene and haloalkylene; R^9 is selected from direct bond and carbonyl, and R^{10} is selected from hydrogen, R^{11}-O-, $(R^{11})_2$N- and R^{11}-(C=O)-NH-, wherein R^{11} is selected from hydrogen and organic groups having 1-20 carbons and optionally containing 1-4 heteroatoms selected from oxygen and nitrogen.

5. A compound of claim 4 wherein R^8 is methylene; R^9 is carbonyl, and R^{10} is $(R^{11})_2$N- wherein R^{11} is selected from hydrogen and organic groups having 1-20 carbons and optionally containing 1-4 heteroatoms selected from oxygen and nitrogen.

6. A compound of claim 3 wherein R^1 is phenyl having a substituent at the position *para* to the site of attachment to the piperazine ring, and the substituent has the formula  , wherein R^{12} is selected from hydrogen and organic groups having 1-20 carbons and optionally containing 1-4 heteroatoms selected from oxygen and nitrogen.

7. A compound of claim 6 wherein R^{12} is selected from hydrogen, alkyl, heteroalkyl, aryl, heteroaryl, carbocycle aliphatic ring and heterocycle aliphatic ring.

8. A compound of claim 7 wherein R^{12} is selected from



9. A compound of claim 1 wherein R^1 is phenyl.

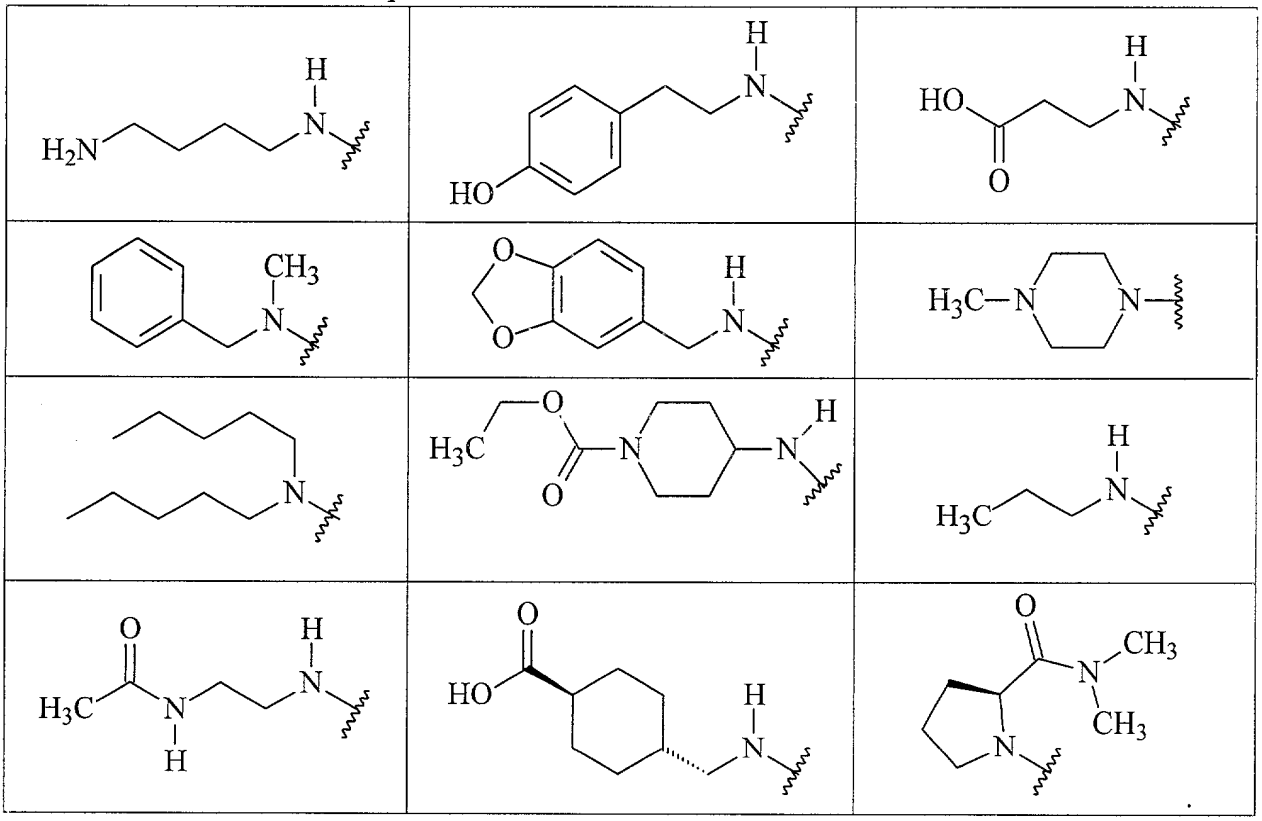
10. A compound of claim 1 wherein n is 1.

11. A compound of claim 1 wherein R^2 and R^3 are independently selected from groups of the formula R^{10}-R^9-R^8-, wherein R^8 is selected from direct bond, alkylene and haloalkylene; R^9 is selected from direct bond and carbonyl, and R^{10} is selected from hydrogen, R^{11}-O-, $(R^{11})_2$N- and R^{11}-(C=O)-NH-, wherein R^{11} is selected from hydrogen and organic groups having 1-20 carbons and optionally containing 1-4 heteroatoms selected from oxygen and

nitrogen, with the proviso that two R^{11} groups bonded to the same nitrogen may be bonded together so as to form a heterocyclic ring with the common nitrogen.

12. A compound of claim 11 wherein R^8 is methylene; R^9 is selected carbonyl, and R^{10} is $(R^{11})_2N$-

13. A compound of claim 12 wherein R^{10} is selected from:

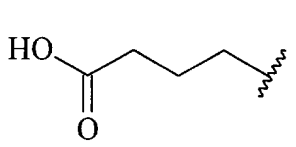
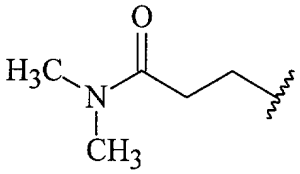
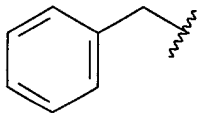
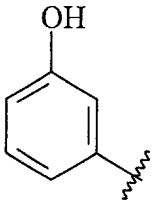
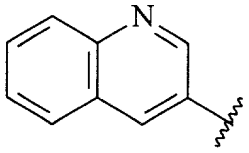
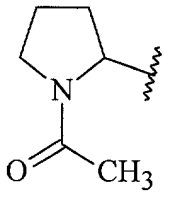
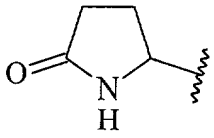
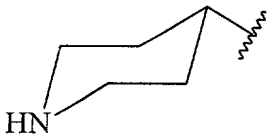
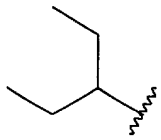
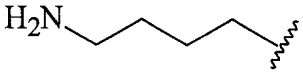
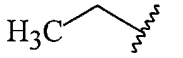
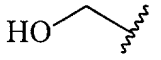


14. A compound of claim 1 wherein R^4 is $-OR^5$.

15. A compound of claim 9 wherein R^5 is selected from hydrogen and alkyl.

16. A compound of claim 1 wherein R^4 is $-NR^6R^7$.

17. A compound of claim 16 wherein R^6 is hydrogen and R^7 is R^{13}-C(=O)- where R^{13} is selected from:

18. A composition comprising a compound according to claim 1 and a pharmaceutically acceptable adjuvant, carrier, diluent or excipient.

19. A method of treating inflammation comprising administering to a subject in need thereof a therapeutically effective amount of a compound according to claim 1.

20. A method for inhibiting a TNF-α mediated processes, comprising administering to a patient in need thereof, through a therapeutically or prophylactically acceptable manner, a therapeutically or pharmaceutically effective amount of a composition comprising a compound of claim 1.

21. A method for inhibiting a TNF-α mediated processes, comprising administering to a patient in need thereof, through a therapeutically or prophylactically acceptable manner, a therapeutically or pharmaceutically effective amount of a composition

comprising a compound of claim 1, wherein the administering is selected from transdermal, oral, intravenous, intramuscular, vaginal, rectal, pulmonary, subcutaneous, sublingual and transmucosal administration.

22. A method for inhibiting a TNF-α mediated processes, comprising administering to a patient in need thereof, through a therapeutically or prophylactically acceptable manner, a therapeutically or pharmaceutically effective amount of a composition comprising a compound of claim 1.

23. A method for treating a condition associated with an elevated level of NFκB activity in a subject, comprising administering to a subject in need thereof an amount of a compound effective to lower the NFκB activity, wherein the compound is a compound of claim 1.

24. A method for treating a condition associated with an elevated level of NFκB activity in a subject, comprising administering to a subject in need thereof an amount of a compound effective to lower the NFκB activity, wherein the compound is a compound of claim 1.

25. A method of inhibiting IL-8 production in a subject in need thereof comprising administering to the subject an effective amount of a compound of claim 1.

26. A method of inhibiting GRO-α production in a subject in need thereof comprising administering to the subject an effective amount of a compound of claim 1.

27. A method for inhibiting a CXCR1 and/or CXCR2 mediated processes, comprising administering to a patient in need thereof, through a therapeutically or prophylactically acceptable manner, a therapeutically or pharmaceutically effective amount of a composition comprising a compound of claim 1.

28. The method of claim 27 wherein the method inhibits a CXCR1 mediated processes.

29. The method of claim 27 wherein the method inhibits a CXCR2 mediated processes.

30. The method according to claim 27 wherein the administering is selected from transdermal, oral, intravenous, intramuscular, vaginal, rectal, pulmonary, subcutaneous, sublingual and transmucosal administration.

31. A method for treating an inflammation event, comprising administering to a patient in need thereof, through a therapeutically or prophylactically acceptable manner, a therapeutically or pharmaceutically effective amount of a composition comprising a compound of claim 1.

32. The method according to claim 31 wherein the administering is selected from transdermal, oral, intravenous, intramuscular, vaginal, rectal, pulmonary, subcutaneous, sublingual and transmucosal administration.

33. A method for identifying a binding partner to a compound of claim 1:

immoblizing proteins known to be involved in the TNF-α signaling pathway onto a suitable carrier; and

passing a solution of said compounds in isolation or mixture over said proteins and analyzing for compound:protein complex formation using surface plasmon resonance (SPR).

34. A method for identifying a binding partner to a compound of claim 1:

providing said compound(s) bound to a solid support to provide solid phase compounds;

contacting a cell or cell components with said solid phase compounds in isolation or mixture;

removing uncomplexed cellular material, for example by gentle washing with aqueous buffer; and

recovering said binding partner from the solid phase compounds.